Nebraska Epidemiology Report

June 2003

West Nile Virus in Nebraska, 2002-2003

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In This Issue . . .

Introduction

The arrival of warm weather heralds the onset of mosquito season. Prior to 2002, mosquitoes were an uncommon vector of human illness in Nebraska. The last outbreak of mosquito-borne viral encephalitis in North America was over 25 years ago (Table 1). Since then, only isolated patients with mosquito-borne encephalitis have been identified. While Nebraska public health officials anticipated West Nile virus (WNV) activity in the summer of 2002, no one anticipated the severity and extent of the outbreak that affected our state last year. The Nebraska count of confirmed, probable, and suspect WNV case-patients was 174, including eight deaths. Our rate of infection in humans and our bird/animal/mosquito surveillance systems suggest that, nationwide, Nebraska was among the most severely affected states last year. Forewarned by last year's experience, Nebraska health care providers should familiarize themselves with this disease and be prepared to diagnose and care for patients infected with WNV.

History

WNV is a single-stranded RNA virus of the Flaviviridae family. The virus belongs to the Japanese Encephalitis Antigenic Complex that includes several other encephalitis-related viruses, such as St. Louis Encephalitis. This can complicate laboratory diagnosis in areas where more than one related virus exists. WNV can be divided into two genetic lineages, only one of which is directly linked to human illness. A strain from this lineage emerged in the United States in 1999 and was identical to a strain found in Israel in 1998.

WNV was originally discovered in the West Nile district of Uganda in 1937. It was identified as a cause of meningoencephalitis in 1957 during an outbreak among elderly patients in Israel. In the early 1960s, it was identified as a pathogen in horses in Egypt and France. The first appearance of WNV in the United States occurred in 1999 in New York. Although the virus had been previously found across

Table 1, West Nile Meningioencephalitis (WNME) North America, 2002: Comparison with other large WNME or St. Louis Encephalitis (SLE) Epidemics

Year	Location	Virus	Number of ME Cases	Number of Deaths	CFR
2002	North America	WN	4,156	284	7%
2000	Israel	WN	240	33	14%
1999	Russia	WN	400	40	10%
1996	Romania	WN	350	17	5%
1975	North America	SLE	2,000	170	8%
1933	USA	SLE	1,400	280	20%

Source: CDC, 2003

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Europe, Africa, the Middle East, and East and Central Asia, this marked its first appearance in the Western Hemisphere.

In 2001, 27 states reported bird or animal cases, but only 66 human cases were reported in ten states. In 2002, 44 states reported confirmed animal or bird cases, and 40 states (including the District of Columbia) reported a total of 4,156 human cases of WNV infection, making this the largest documented mosquito-borne arbovirus epidemic in the Western Hemisphere.

Clinical Description

WNV is most often transmitted to humans through the bite of infected mosquitoes. It has an incubation period ranging from 3-14 days. The vast majority of WNV infections are asymptomatic, with a ratio of symptomatic to asymptomatic cases of approximately 1:140. The differential diagnosis for WNV meningitis/encephalitis includes: enteroviruses, other arboviruses, herpesviruses (HSV 2, HSV 1, EBV, HHV 6, VZV), HIV, lymphocytic choriomeningitis, mumps, Lyme disease, leptospirosis, secondary syphilis, partially treated bacterial meningitis, parameningeal disease, tuberculosis, cryptococcus, autoimmune disease, and medication-related aseptic meningitis.

There is a spectrum of illness in symptomatic persons infected with WNV. While estimates of the distribution of infected patients falling into various diagnostic categories are crude, experts suggest that approximately 80% are asymptomatic, 20% suffer from WNV fever, and less than 1% develop encephalitis and meningitis. The spectrum of WNV illness includes:

West Nile virus fever: An incompletely defined syndrome that includes a febrile illness of sudden onset, often accompanied by fatigue, malaise, anorexia, nausea, vomiting, eye pain, headache, and myalgia, lasting 3 to 6 days.

Meningitis/encephalitis: These more severe neurologic manifestations of WNV infection are clinically comparable to other forms of viral meningitis/encephalitis. Meningitis indicates meningeal inflammation (headache *plus* true nuchal rigidity, photo/phonophobia, and pleocytosis). Encephalitis includes identifiable neurologic deficits, ranging from focal neurologic signs (cranial nerve abnormalities, abnormal reflexes) to more global neurologic dysfunction (disorientation, confusion, coma, etc).

Movement disorders: A polio-like paralysis consistent with anterior-horn cell disease that may occur in the absence of meningoencephalitis systems, and may persist as a chronic disability; myoclonus; Parkinson's-like symptoms; severe muscle weakness; Guillain-Barre syndrome.

Death: Nebraska experienced eight deaths attributed to WNV infection last year. While fatalities conformed to reported high risk profiles (elderly, immunocom-promised), Nebraska recorded the youngest fatality reported nationwide, a 19 year-old male with no reported underlying illness.

Because this disease has only recently emerged in the Western

Hemisphere, the full range of clinical illness associated with WNV continues to be defined. Additional clinical scenarios suggested to be associated with this infection include: flaccid paralysis with sensory symptoms (neuropathic pain, causalgia, paresthesias), peripheral neuropathy, polyradiculopathy, optic neuritis, acute demyelinating encephalomyelitis; prenatal WNV infection with CNS developmental abnormalities. Physicians seeing patients with symptoms such as these should consider the possibility of WNV infection, and pursue appropriate diagnostic testing.

Treatment

There is currently no known treatment for WNV infection. Research protocols may be available for patients with severe or life-threatening illness. Supportive care, including hospitalization and prevention of secondary infections, is critical. WNV human vaccines have been discussed but are not currently available.

Who is at Risk

Mosquito-exposed Persons:

All residents with mosquito exposure in areas where WNV has been identified are at risk for becoming infected with the virus. People over the age of 50 are at an increased risk for serious illness and death. Recent mosquito surveys and human serosurveys in areas where the largest outbreaks of WNV disease have occurred suggest that a relatively small percentage of mosquitoes actually carry the virus, and that seroprevalence in human populations is less than 5%. The Nebraska Health and Human Services System (NHHSS) has a regularly updated website that can be used to track the spread of the virus, and identify areas of risk. (http://www.hhs.state.ne.us/wnv/)

Incidental Exposure:

In addition to mosquitoes, some less frequent means of WNV transmission have been identified. WNV can be transmitted through blood transfusions and organ donations. Physicians should report to public health authorities any patient with WNV infection occurring within four weeks after receiving a blood transfusion or organ donation. There are isolated reports of WNV transmission from a mother to her unborn infant, transmission from mother to child through breast feeding, and transmission from accidental puncture wounds from contaminated laboratory instruments.

Case Classification

Persons with WNV infection are classified as suspect, probable or confirmed. Persons living in an area where WNV activity has been reported (human, animal, or insect) who develop symptoms matching those commonly associated with WNV but lacking CDC-recognized serologic or other laboratory confirmation of WNV infection are suspect cases. Every effort should be made to confirm these with an approved laboratory test. Suspect cases are not reported to or counted by the CDC.

A probable WNV case is any person with a clinical illness compatible with WNV disease, as described above, occurring during a period when arboviral transmission is likely, in an area where WNV activity has been reported (human, animal, or insect), and with the following supportive serology: 1) a single or stable (less than or equal to twofold change) but elevated titer of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

A confirmed WNV case-patient is any person with:
a fourfold or greater change in virus-specific serum antibody titer; or isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid; or virus-specific IgM antibodies demonstrated in CSF by antibody-capture EIA; or virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum IgG antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

2002 Nebraska WNV Surveillance

Humans:

Nebraska had a total of 174 suspected, probable or confirmed patients with WNV infection, the eighth highest in the country. The majority of patients were over 30 years old; 72% were between 30 and 75 years of age

Table 2, Snapshot of Reported West Nile Virus Illness in Nebraska, 2002

Total Human Patients	174
Total Deaths	8
Number of Males with Virus	98
Number of Females with Virus	76
Number of Fatal Male Cases	6
Number of Fatal Female Cases	2
Average Age with Virus	52.5
Average Age of Deceased	69
Average Age of Survivors	51.7
Youngest Deceased	19
Oldest Survivor	93

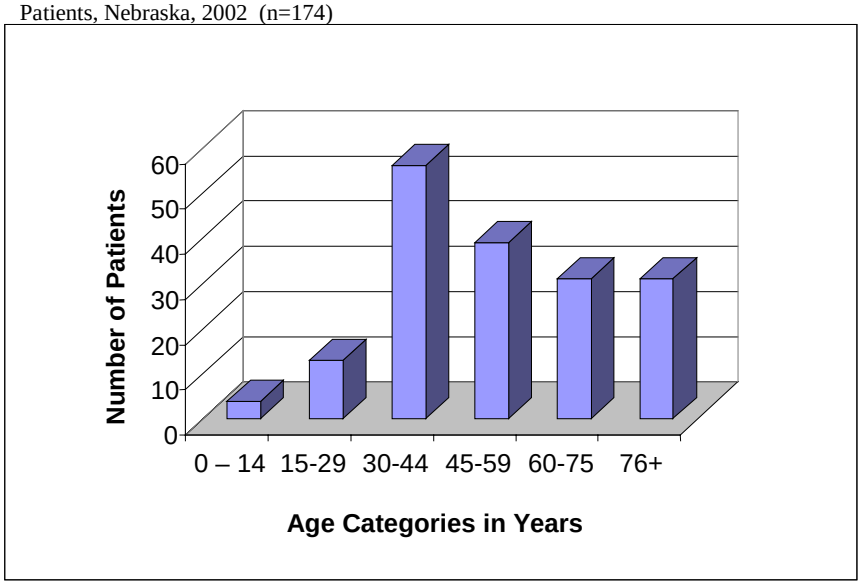
Source: Nebraska Health and Human System, 2003

(Figure 1). The first patient had symptom onset on August 4. The weekly number of reported patients rose steadily and peaked during the week of September 8, with 39 cases. The latest reported patient had symptom onset on October 15 (Figure 2).

The severity of illness in Nebraska's 174 case-patients ranged from a relatively mild febrile illness to death. Of the 174, 86 (49 %) had either an afebrile (n=19) or febrile (n=67) viral syndrome of mild-to-moderate severity. The remaining 88 patients had meningitis (n=44, 25%), or encephalitis (n=44, 25%). In total, there were eight (n=8, 5%) fatal WNV human cases in Nebraska for 2002. While seven of the eight fatalities were elderly, one of the eight was a 19-year-old patient, the youngest WNV-related fatality in the United States in 2002.

Of Nebraska's 93 counties, 48 reported human WNV infection. Figure 3 shows the number of total WNV case-patients and fatalities for each county. While WNV affected all parts of the state, most human cases occurred in the eastern and central parts of the state. When adjusted for population, the central region of the state was most severely affected. In the Panhandle, only Scotts Bluff County reported human WNV infection (n=6, 2 fatalities).

Figure 1, Age Distribution of Suspected, Probable or Confirmed West Nile Virus Patients, Nebraska, 2002 (n=174)

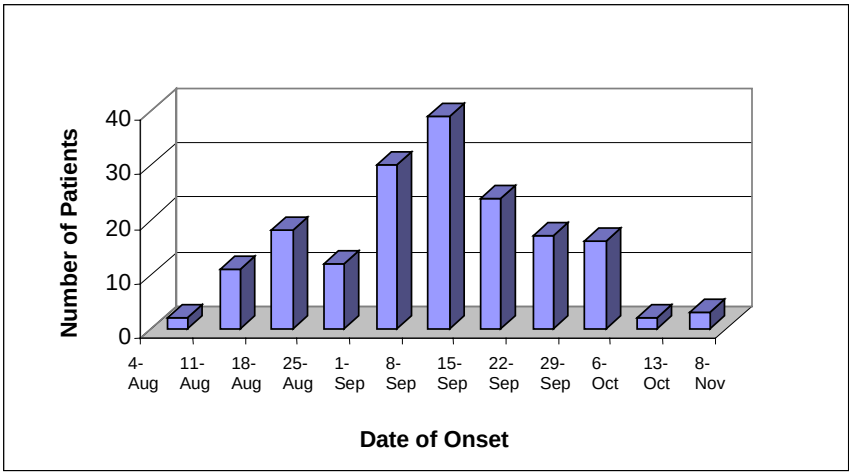


Source: Nebraska Health and Human Services System, 2003

Non-Human Surveillance:
In addition to surveillance of human cases, NHHSS and the local health departments monitored for the presence of WNV in mosquitoes, birds, horses, and other animals. Surveillance in non-human sources was critical in forecasting risk for humans. Mosquitoes and birds are critical targets for WNV surveillance as these agents are directly involved in the transmission cycle. Horses, like humans, develop WNV disease later in the season, but are widely exposed to potentially infected mosquitoes and serve as a valuable index for WNV activity.

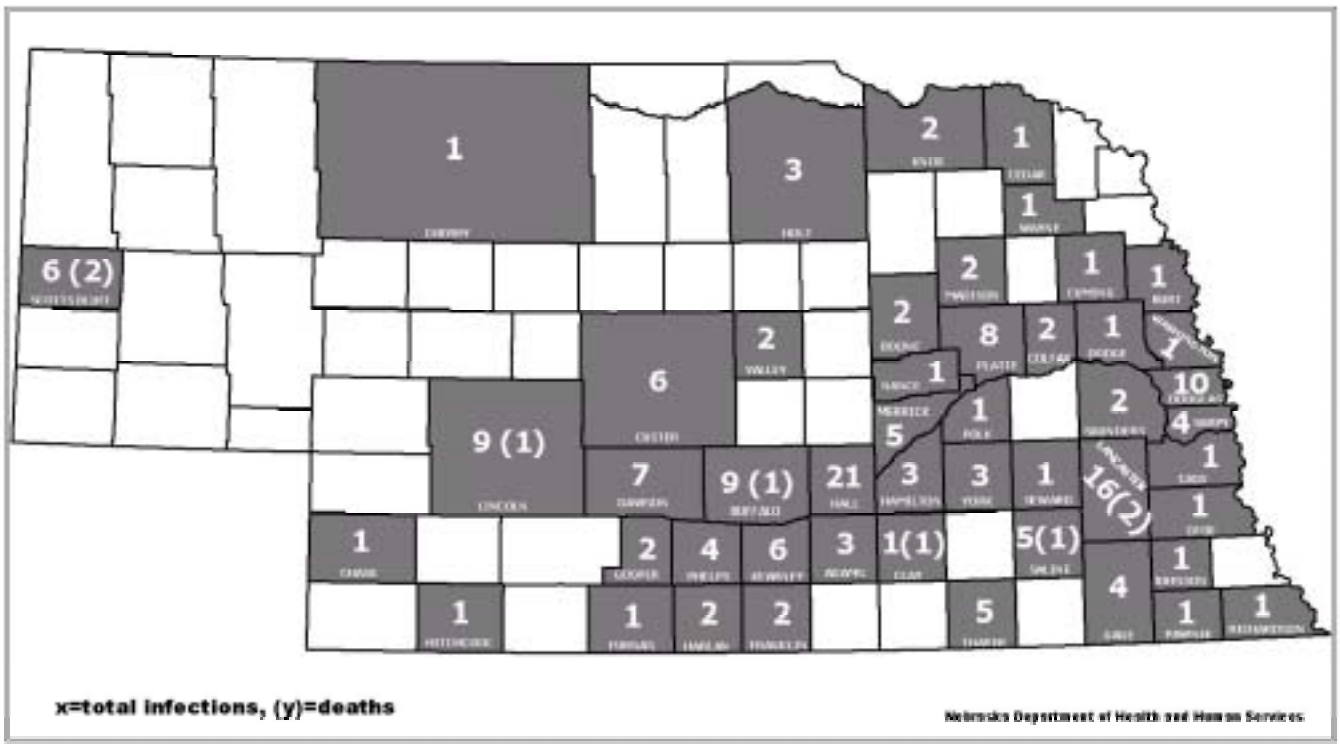
Bird Surveillance:
Dead birds are one of the first signs of WNV activity, and typically precede human and equine disease. Dead birds, and infected birds displaying erratic behavior, are highly visible, enabling casual observers to identify and report areas where WNV may be active. In 2002, 866 dead birds were tested, of which 511 (59%) were positive for WNV. Birds were tested from 83 of Nebraska's 93 counties: 71 (76%) reported at least one positive dead bird. The first WNV positive bird was identified in Lancaster County on June 28, 2002, more than a month before the first human case was detected (August 4). Over the next month, WNV infection was identified in dead birds from across the state.

Figure 2, Nebraska Human West Nile Virus Cases by Week of Onset, Nebraska, 2002 (n=174)



Source: Nebraska Health and Human Services System, 2003

Figure 3, Geographic Distribution of Human West Nile Virus Patients (n=174) and Deaths (n=8), by County (n=48), Nebraska, 2002

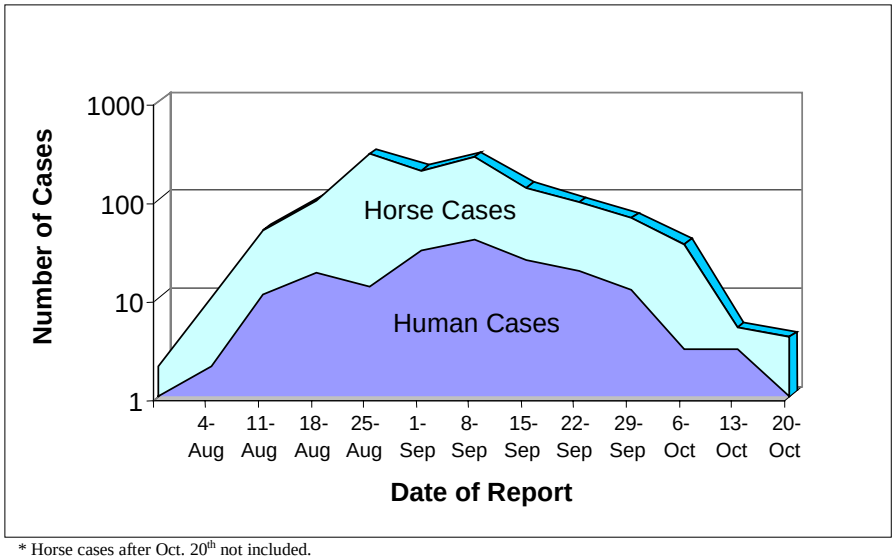


Mosquito Surveillance:
Additional WNV surveillance included testing of pools of mosquitoes from locations across the state. Mosquitoes were routinely collected in seven counties and supplemented by selective sampling in nine additional counties. Mosquitoes were trapped overnight and sorted by sex into common species-pools of 1 to 50 mosquitoes. In 2002, of the 1,147 pools (36,561 individual mosquitoes) tested, 242 pools (21%) were positive. In Dawson County, where seven human WNV case-patients were reported, 121 of 211 (57%) of the mosquito pools were positive, the highest rate of any county.

Equine Surveillance:
A total of 1,100 equine WNV infections were reported to the Department of Agriculture, from 92 of Nebraska's 93 counties, the third largest number among all states, behind Texas and Illinois. Infection in horses and humans appears to occur concurrently. For instance, Nebraska's first equine WNV infection was reported in Lancaster County on August 6, two days after the first human case, also in Lancaster County. While surveillance for WNV in horses is unlikely to provide a substantial advanced warning of human risk (Figure 4), their more extensive outdoor exposure makes them a useful component of our WNV surveillance system.

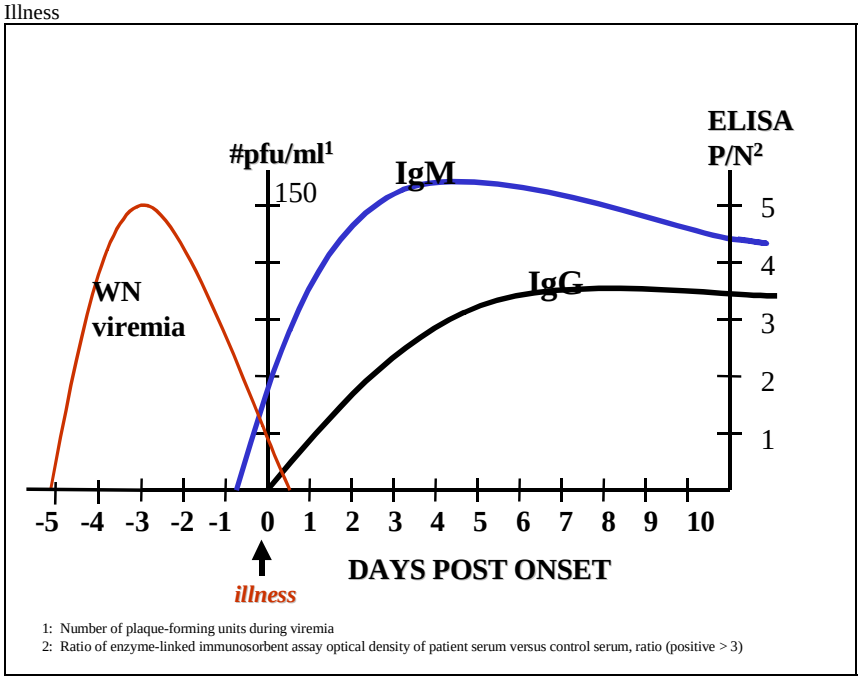
Sentinel Chicken Flocks:
NHHSS established 19 sentinel chicken flocks of six birds each as an additional surveillance tool in

Figure 4, Log Scale Distribution of Human vs. Equine West Nile Virus Disease, by Week of Onset, Nebraska, 2002 (n=174/1078*, human/horse respectively)



* Horse cases after Oct. 20th not included.
Source: Nebraska Health and Human Services System, 2003

Figure 5, Chronology of WNV Viremia and IgM/IgG Antibody Response in Relation to Onset of Illness



Source: CDC, 2003

2002, but with limited success. Chickens can be infected with the WNV and produce detectable levels of antibodies, but they do not become clinically ill, nor do they produce sufficient virus to perpetuate the transmission cycle. The 19 sentinel chicken flocks were placed in seven counties. Of the 877 serum samples, only five (0.5%) were positive. While one of the positive serologies (July 23) preceded the first reported human WNV illness, the small number of positive results limited the utility of these flocks as a surveillance tool. The low seroprevalence in the sentinel chicken flocks may be attributable to the 14 day testing interval, as recent studies indicate that IgM serum levels in chickens peak as soon as seven days after infection.

2003 Human WNV Reporting and Laboratory Testing

To ensure timely and accessible WNV laboratory diagnostic testing, Nebraska public health authorities have established diagnostic testing services for WNV infection at the Nebraska Public Health Laboratory (NPHL). The recommended test to diagnose WNV infection is the "IgM capture ELISA" performed on either CSF or serum. IgM antibody is commonly present in patients around the time of onset of symptoms. Figure 5 illustrates the relation of IgM and IgG levels to the onset of viral infection and symptoms. **However, not all patients will be positive for IgM antibody at the time of initial visit.** If the initial test is negative, clinicians should consider a "convalescent" IgM capture ELISA test, collected at least 14 days following the onset of symptoms. While seroconversion is the most reliable indication of acute WNV infection, patients who fit the clinical profile and whose "acute" titer is positive meet our epidemiologic case definition of a "probable" case. NPHL will not be performing WNV **IgG** antibody tests, but such testing can be arranged on a case-by-case basis by contacting a public health epidemiologist for your jurisdiction.

The IgM capture ELISA test will be available at the NPHL. NHHSS has obtained limited funding from the Centers for Disease Control and Prevention to address the need for human WNV testing. While the demand for human WNV testing is unknown, we hope to be able to cover the cost of IgM capture ELISA testing for the duration of the WNV season. **No testing for WNV other than the IgM-capture ELISA will be available through the NPHL. The cost of WNV tests other than IgM capture ELISA will accrue to the patient, third-party payer or health care provider.** Should demand for testing exceed available resources, we will notify Nebraska health care providers and laboratories of the need to charge the "IgM capture ELISA test. The test will continue to be available to anyone for a cost of $50 throughout the WNV season at the NPHL. Specimens can be routed through any Nebraska laboratory, or can be sent directly to the NPHL. A copy of the test requisition is included with this mailing, and can be photocopied as needed. Additionally, a copy of the requisition can be downloaded from the NHHSS West Nile website (http://www.hhs.state.ne.us/puh/epi/wnv/healthpros.htm). Testing can be performed on either serum (0.5 ml minimum) or CSF (1.0 ml minimum) and should be kept cool (4° C) but not frozen. The CDC will perform confirmatory testing on a sample of Nebraska specimens to confirm the results of NPHL testing. This confirmatory testing is necessary to differentiate WNV infection from that caused by related arboviruses (Western Equine Encephalitis, and St. Louis Encephalitis virus).

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UNIVERSITY OF NEBRASKA MEDICAL CENTER
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PHONE: (402) 559-2440 FAX: (402) 559-9497

SPECIAL MICROBIOLOGY REQUISITION

PATIENT LAST NAME | FIRST NAME | MI

SUBMITTED BY:

DATE OF BIRTH / / | AGE | SEX M / F

ADDRESS | APT

CITY | STATE | ZIP

COUNTY CODE **STATE CODE** **SURVEILLANCE SITE**

PHYSCIANS NAME | PHONE #

COLLECTION DATE / / | **COLLECTION TIME** **AM / PM**

STATE APPROVAL BY:

ID / CHART NUMBER (NUMBER WILL APPEAR ON REPORT)

Clinical Diagnosis:_____ **ICD 9 Code:**_____

Race ___White ___Black ___Native American ___Asian/Pacific Islander ___Unknown ___Other_____

Ethnicity ___Hispanic ___Non-Hispanic ____Unknown

SPECIMEN FOR CULTURE

Source: _____Bronchial Aspirate _____CSF _____Genital _____Nasopharyngeal _____Sputum _____Stool _____Throat _____Urine _____Blood _____Other _____

Bacteriology
____Enteric Pathogen Culture
____*Escherichea coli* O157:H7 Culture
____*Bordetella pertussis* Culture
____*Bordetella pertussis* DFA
____*Corynebacterium diphtheria* Culture
____Group A *Streptococcus* Culture
____*Legionella* Culture
____*Legionella* DFA
____*Clostridium difficile* Toxin

Mycobacteriology ____AFB Culture and Smear, **Initial** ____AFB Culture and Smear, **Follow-up** ____AFB Susceptibility Testing

Mycology ____Fungus Culture ___Cryptococcus Antigen

Virology **_____West Nile Virus IgM Capture ELISA**

Parasitology Recent Travel: ____No _____Yes, specify _____
____Ova and Parasites ____Giardia _____Tick Identification _____Worm Identification _____Other:_____

REFERRAL

Source: _____Bronchial Aspirate _____CSF _____Genital _____Nasopharyngeal _____Sputum _____Stool _____Throat _____Urine _____Blood _____Other_____

Date of Isolation:_____
Recovery medium:_____ **Transport medium:**_____
Preliminary Identification (Gram stain, morphology, biochemical tests performed):

ORGANISM

____Confirmation / Identification
____*Escherichia coli* O157:H7 ____*Salmonella* species ____*Shigella* species ____*Campylobacter* species
____*Haemophilus* ____*Neisseria* species ____*Mycobacterium* species ____Other_____

____ **Antibiotic Resistance Confirmation** _____MRSA _____VRE _____ESBL _____Other_____
____ **Sterotyping/Serogrouping** _____*Salmonella* species _____ *Shigella* species _____*H. influenzae* _____ *N. meningitidis*

___ **Organism Banking** Organism identified as:_____

CDC has recognized WNV testing from at least one commercial laboratory as capable of diagnosing WNV infection in a fashion comparable to that developed by CDC and disseminated throughout state public health laboratories: Focus Technologies Laboratory (http://www.focusanswers.com/).

Clinicians choosing to use other laboratories offering WNV diagnostics should check with the laboratory to be sure that CDC has deemed their testing methodologies/results comparable to standard CDC WNV tests.

All persons suspected of WNV infection should be promptly reported to a public health epidemiology office. Epidemiology staff will facilitate the processing of laboratory specimens.

Physicians, laboratories and hospitals are required by state regulations to report mosquito-borne encephalitis, including WNV. For physicians in Douglas County, call the Douglas County Health Department; in Lancaster County, call the Lincoln-Lancaster County Health Department; for all other counties call the Office of Epidemiology at NHHSS (Figure 6). Please be prepared to report demographic information (name, age, sex), description of illness, and hospitalization history.

2003 Surveillance and Public Health Response

As WNV becomes endemic in Nebraska, NHHSS will target future surveillance and control efforts toward areas of greatest risk and to the mosquito and animal species most involved in the disease cycle.

When WNV is first detected in Nebraska in 2003, NHHSS will immediately inform the local health departments, followed by the transmission of faxed information to hospitals, physicians, veterinarians, and other health care providers.

To contact a public health official regarding West Nile Virus:

Douglas County Health Department:
Work Hours…..…..(402) 444 – 7214
After Hours…….(402) 444 – 7000

Lincoln-Lancaster County Health Department:
Work Hours…...….(402) 441 – 8053
After Hours…….(402) 441 – 8000
(Request Communicable Disease Program)

Nebraska Health and Human Services System - Office of Epidemiology:
…….(402) 471 – 2937

Figure 6, Resources fo
Infection and Ordering
Tests

NHHSS will also provide information to the news media to inform the public of the risk of the disease, disease symptoms, personal protective measures, and environmental control measures. Local health departments will reinforce these messages and supplement them with additional information targeted to their specific communities.

NEBRASKA HEALTH AND
HUMAN SERVICES SYSTEM
DEPARTMENT OF REGULATION AND LICENSURE
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LINCOLN, NE 68509-5007

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